New technology helps to find gene responsible for Kufs disease

May 5 2011

Professor Sam Berkovic, from the University of Melbourne, Australia, said the discovery of the gene at the root of the brain disorder, Kufs type A disease, will enable us to use a rapid and simple blood test to genetically test for the disease. Credit: Gavin Blue/The University of Melbourne

Scientists from the Walter and Eliza Hall Institute and the University of Melbourne have used innovative new technologies to identify the gene responsible for a rare but fatal hereditary brain disorder. The discovery will make it possible to diagnose the disease through a blood test rather than a brain biopsy.

Dr Melanie Bahlo, Ms Katherine Smith and Ms Catherine Bromhead from the Walter and Eliza Hall Institute's Bioinformatics division, in collaboration with neurologist and epilepsy specialist Professor Sam Berkovic and Dr Todor Arsov from the University of Melbourne, have

found that mutations in the CLN6 gene on chromosome 15 are the cause of inherited recessive Kufs type A disease. The paper was published in the American Journal of Human Genetics.

Kufs disease is a rare but fatal, hereditary neurodegenerative disease usually identified in early adulthood. Brain symptoms result from a build up of fat in brain cells that is toxic to the cells, causing symptoms including epilepsy, dementia, impaired motor function and intellectual deterioration. It affects approximately 1 in 1,000,000 people.

Professor Berkovic, head of the Epilepsy Research Centre at the University of Melbourne and the Comprehensive Epilepsy Program at Austin Health, said identification of the CLN6 gene would enable more efficient and much less invasive techniques for earlier diagnosis of Kufs disease.

"Currently, the only way that we can reliably diagnose this disease is to do an invasive and dangerous brain biopsy, or at autopsy," Professor Berkovic said. "The discovery of the gene at the root of Kufs type A disease will enable us to use a rapid and simple blood test to genetically test for the disease. It will also give us the ability to screen for the disease in people in at-risk families, and make it possible for genetic counseling, which we already know to be very important for patients."

Dr Bahlo's and Ms Smith's innovative work used data generated from a person's DNA, called SNP genotyping. When combined with sophisticated mathematical and statistical analysis, the information helped them identify the region in the human genome likely to contain the DNA error that causes Kufs disease which led to discovery of the gene mutations.

"The genetic cause of Kufs disease has remained a mystery for over 25 years, because the rarity of the condition meant that our patient groups

were so small we couldn't reliably pinpoint any particular genetic mutations that caused their disease," Dr Bahlo said. "In this study, we used an innovative suite of highly specialised techniques and statistical algorithms that compensated for the small sample size and allowed us to look at the entire genetic code of people with Kufs disease to find which region of the DNA had the mutation which caused disease. Discovering the CLN6 gene as the cause of Kufs disease is a great outcome for us and for the people who are affected by this awful disease."

Professor Berkovic said the best possible outcome from the study would be the development of a treatment for Kufs disease, which is currently untreatable and invariably fatal. "The general aim and hope of this work is always to be able to use the discovery to translate to a treatment, but this is still some time away," he said.

Professor Berkovic said that his team's collaboration with Dr Bahlo's bioinformatics group at the institute had produced several exciting results in a short time. This includes a number of important outcomes for epilepsy sufferers, with the genetic basis for four epilepsy-related diseases discovered in the past four years.

Dr Bahlo said that the innovative study used to find the gene responsible for Kufs disease could hold the key for finding the genetic cause of a number of other hereditary diseases including other epilepsy-related diseases, deafness and some familial cancers.

"These new techniques for using statistical data and mathematical algorithms to track down the genetic basis of disease are really at the forefront of medical research today," Dr Bahlo said. "Finding the genes responsible for certain diseases will help us in our quest to generate new diagnostic tools as well as provide the basis for fundamental biology that leads to development of new drugs and therapies to treat disease."

Provided by Walter and Eliza Hall Institute